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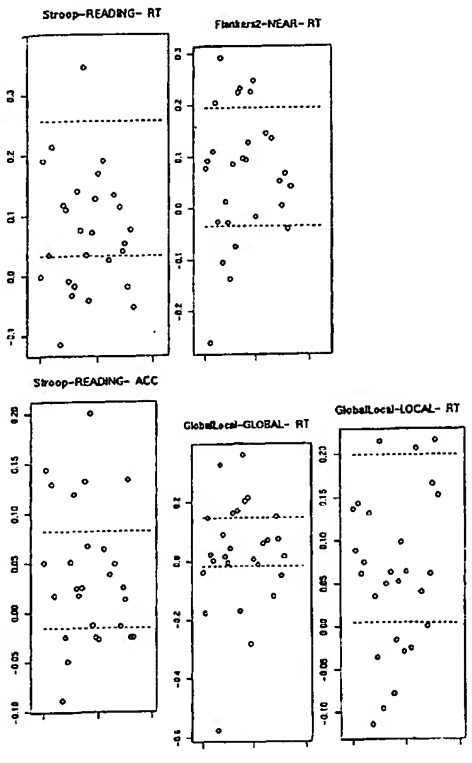

(57) Abstract: The invention relates to a method for diagnosis and for treatment of ADHD and ADD (Attention Deficit Disorder), based on computer-generated visual stimuli. The invention additionally relates to a system for use thereof.

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A METHOD AND SYSTEM FOR DIAGNOSIS AND TREATMENT OF ADHD AND ADD

FIELD OF THE INVENTION

The present invention generally relates to the field of Attention Deficit Hyperactivity Disorder (ADHD). More specifically, the invention relates to a method for diagnosis and for treatment of ADHD and ADD (Attention Deficit Disorder), based on computer-generated visual stimuli. The present invention additionally relates to a system for use thereof.

BACKGROUND OF THE INVENTION

Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral disorder among children. It is most often noted at pre-school or school age, when a child is seen to be "unfocused" and impulsive compared with his/her peers. The child is typically restless and has a short attention span, finding it difficult to ignore distractions and concentrate on instructions. Often, the child is aggressive and exhibits frequent temper tantrums. Fine motor skills may be impaired, which increases their difficulties with writing. It is estimated that 3-5% of school-age children are affected with the disorder (NIH Consensus Statement 1998 Nov. 16-18; 16(2): 1-37); other sources quote a prevalence of up to 12%. In adolescence, symptoms of hyperactivity seem to decline, however inattention and impulsiveness remain, resulting in poor academic performance. Approximately 35% of ADHD children in the U.S. do not graduate high school. Low self-esteem is common among these teens, and 25-30% of ADHD adolescents exhibit anti-social behavior, or associate with other problem teens. Approximately half of ADHD children demonstrate symptoms in adulthood as well.

ADD is similar to ADHD, in that symptoms of inattention are manifested, however hyperactivity is not apparent.

Three subtypes of ADHD are recognized by the DSM-IV (Diagnostic & Statistical Manual of Mental Disorders (DSM) from the American Psychiatric Association), characterized according the predominance of: 1) inattention, (subtype ADHD/IA) 2) hyperactivity/impulsiveness, (subtype ADHD/HI) or 3) both (subtype ADHD/COM) (J. Abnormal Child Psychol. 29, 189-205, 2001). Treatment approaches may be tailored according to the behavior exhibited (i.e., inattention or hyperactivity/impulsivity).

Methods of treatment which are in widespread use include administration of psychotropic drugs, in particular administration of Methylphenidate (RITALIN.RTM.), and psychosocial treatment intended to encourage behavioral change. Ritalin is generally more effective than tricyclic antidepressants (eg, imipramine), caffeine, and other psychostimulants (eg, pemoline and deanol) and has fewer side effects than does dextroamphetamine. Administration of ritalin decreases the overt symptoms of hyperactivity, however does little to improve academic or social skills. The effects of the drug tend to wear off two to three hours after it is taken. Common side effects of methylphenidate are sleep disturbances (eg. insomnia), depression or sadness, headache, stomachache, suppression of appetite, elevated BP, and, with large continuous doses, a reduction of growth. Some parents are concerned with the stigma attached to medicating a child. Psychosocial treatment, when instituted in the classroom or at home, tends to include reward systems, timeouts, response-cost training, and has been shown to be beneficial, though patience is required of the teacher and parent. (NIH Consensus Statement 1998 Nov. 16-18; 16(2): 1-37).

No single standard exists for the diagnosis of the disorder, which leads to incidents of both over-diagnosis and under-diagnosis of the disorder. Literature notes that 20-40% of ADHD children are misdiagnosed as being false-negative for the disorder, and consequently they do not receive treatment from which they would have benefited. Commonly, diagnosis is given based on an interview with the child and his parents; questionnaires may be used, and the evaluation is performed by either a family practitioner, a pediatrician, a psychologist, a neurologist or a psychiatrist. Such an interview can be highly subjective, with the personality and prejudices of the doctor, and the patient or parent, playing an underlying role. Family practitioners tend to diagnose more quickly and to prescribe medication more readily than pediatricians or mental health caregivers. In addition, one or more tests may be administered to aid in the diagnosis, with the object of these tests being to measure how long the child can maintain their attention and how impulsive they can be over time. One type of test widely used is the "Continuous Performance Test" (CPT), an example of which is Conners' Continuous Performance Test. The most common CPT requires the participant to observe a screen while single letters or numbers are

presented onto it at rapid pace. The child is told to respond (e.g., by pressing a key), when a certain stimulus or pair of stimuli in sequence appears. Several scores are derived from the CPT: the rate of correct responses, the standard deviation of the reaction time (of correct responses), the rate of target stimuli missed (omission errors), and the rate of responses following nontargets (commission errors).

Another test used is the Stroop test, described in 1935 by John Ridley Stroop. He coined the term "associative interference", to explain the difficulty of people in naming the ink colors of incongruent words (for example, naming aloud the color "green" in which the word "red" is printed). He showed that on the average it took 74% longer time (47 seconds) to name the colors of 100 incongruent color words than to name the color of 100 solid squares. This marked interference response has been termed the "Stroop effect." ADHD children take longer than healthy children to complete the Stroop test, and are less able to ignore the interference.

Other tests used in diagnosis are: the Integrated Visual and Auditory Continuous Performance Test (IVA), the Gordon Diagnostic Systems, Yale Children's Inventory (YCI), the Attention Battery (which includes Continuous Performance Task Progressive Maze Test and Sequential Organization Test (SOT), the Wechsler Intelligence Scales for Children (WISC-R), T.O.V.A - Test of Variables of Attention, the Learning Efficiency Test II (LETT-II), the Developmental Test of Visual Motor Integration (VIM), Wide Range Achievement Test (WRAT-R).

US Pat. No. 6,053,739 discloses a computer-displayed attention performance test for diagnosis of ADHD. US Pat. No. 5,377,100 discloses a method of treatment for ADHD, based on the principles of biofeedback. In this patent, a child plays a flight simulating video or computer game, and the child's attention level is monitored via EEG measurements. When a reduction in attention level is sensed, a sign is displayed on screen, and the child is meant to respond by refocusing his/her attention. The level of difficulty of the game is adjusted automatically according to the child's performance, in order to attract his attention. In US Pat. No. 5,377,100, attention is treated as a single entity, the level of which can be measured by EEG, however, it is not widely accepted that EEG measurements such as those described, are correlated with attentional performance.

The diagnosis of ADHD is made more problematic by the fact that input from the parents is more often relied upon as the major data source, with less weight being given to teacher input or to input from the child himself. Additional disorders exist which mimic the symptoms of ADHD: learning disabilities, depression and mental retardation. The need exists for a thorough evaluation tool, which can be used to diagnose ADHD in a reliable, reproducible and scientific manner. Such a tool should highly limit the incidence of misdiagnosis, and preferably should supply the examiner with knowledge that would pinpoint the areas most problematic for each child undergoing evaluation. This would ease the treatment regimen- allowing it to be tailored to fit each ADHD sufferer.

Certain schools of thought classify the aspects of attention that can be impaired in ADHD children. "Attention", or rather "lack of attention", is not seen as a single fault present in ADHD children. According to the doctrines of visual attention and cognitive neuropsychology, the attentional system is based on several distinct entities of attentional function. The inventors of the present invention claim that all or some of the following four attentional functions can be impaired in each ADHD sufferer:

1. Sustained attention- the ability to allocate sufficient attentional resources for extended periods of time without activating the response system. Maintaining a high level of alertness, avoiding mental drifts and lapses.
2. Selective attention- the ability to focus attention on relevant information while ignoring distracting information regardless of its salience or attractiveness. This is important, for instance, in a noisy classroom situation, when the child must nevertheless focus on the teacher.
3. Orienting of attention- the ability to direct one's visual focus to a specific area in the visual field, and to disengage and reorient the visual focus to another area in the visual field. Impairment in this aspect of attentional function, would be expressed in a school-age child as difficulty in reading and in mathematics.
4. Control of attention- the ability to integrate and oversee all of the aforementioned attentional functions. The ability to co-ordinate one's attention and successfully organize and accomplish tasks. Shifting between different modes of attention (e.g., focused, divided, defused).

The inventors of the present invention have developed a novel and comprehensive assessment tool for diagnosing ADHD and a training approach for

treating ADHD. The assessment tool is comprised of a series of computer-generated visual tasks, each one related to one of these four aspects of attentional function. These visual tasks are used to create an "attentional profile" for each subject tested; this profile indicates which aspects of attentional function are impaired in the subject tested and to what extent, and this data can be used to design a treatment program suited for that particular individual. Prior art methods and systems, which use single tests, are limited and not comprehensive enough. For instance, the continuous performance tests performed in the prior art, (such as the Connors, Gordon and T.O.V.A. tests), are influenced by the child's memory function, and his intelligence, neither of which reflects the level of function of the child's attention. In prior art single tests, a child who is behaviorally uncooperative or apathetic will score poorly on the test, even though his attentional capabilities may be normal on another given day, when he is not moody. Any single one of the tasks alone (even those disclosed in the present invention, which are more suited to ADHD children than prior art single tests) is not enough to provide an accurate diagnosis. However, when the entire ensemble of tasks described here, some of which are entirely novel, is used to establish a profile of the patient, the diagnosis is extremely accurate and addresses all areas of the disorder. This is due to the inclusion of an entire regimen consisting of different types of tasks, each of which relates to one of the four entities of attentional function. The treatment program designed for each child, based on the resultant attentional profile, is more satisfactory as well and highly specific to the patient. It is the object of the present invention to provide a computer-based method of diagnosis and a method of treatment of ADHD. The method of diagnosis is both reproducible and reliable, having much fewer "false negative" and "false positive" incidents of misdiagnosis than the diagnostic practices common in the art today. The method of treatment is shown to substantially improve reading comprehension, mathematical skills, passage copying and organizational skills of school-age children, after fewer than 20 training sessions. The methods of the present invention eliminate the subjectivity usually involved in testing for ADHD and provide a total, and objective assessment of the patient. Additionally provided is a system for use in diagnosis and treatment of ADHD. These and other objects of the present invention will become more apparent from the detailed description of the invention below.

DEFINITIONS

For the sake of brevity, in the present invention the terms "ADHD" and "attention deficit hyperactivity disorder" will be used to include and encompass ADD (attention deficit disorder) as well.

In the present invention, the term "attentional profile" refers to an overall scheme describing the extent in which each child deviates from the aged matched norm in each of the four attentional functions.

In the present invention, the patient undergoing diagnosis or treatment for ADHD is sometimes referred to as a child, since most often the disorder is diagnosed during childhood; however there is no intention to limit the scope of the present invention for use in children only. The methods and the system for diagnosis and treatment can be used for all ages.

SUMMARY OF THE INVENTION

There is thus provided in the present invention, a method for comprehensive and sensitive diagnosis of Attention Deficit Hyperactivity Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli; and said computer generated visual stimuli are comprised of at least nine tasks selected from the following types of task: a sustained attention test, a visual search, a flanker task, a cost-benefit paradigm with endogenous cues, a cost-benefit paradigm with exogenous cues, a stroop task, a stroop-like task, a global-local task or a switched global-local task;

b) measuring the response time and accuracy of response of the patient for each of said tasks;

c) comparing said measurements for each task with measurements generated from healthy individuals;

d) generating an attentional profile for the patient based on said comparison;

e) diagnosing the presence or absence of ADHD or ADD in said patient.

According to a preferred embodiment, the method additionally comprises a standardization step of computing attentional calculations from said response time and accuracy of response measurements, and said attentional calculations are utilized in step (c) in said comparison. In certain embodiments of such case, in each task, at least one of a plurality of attentional calculations is selected for use, according to the nature of said task.

The is also provided in the present invention, a method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli;
b) measuring the response time and accuracy of response of the patient to said visual stimuli;
c) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;
d) adjusting the level of difficulty of said visual stimuli according to the response times and accuracy of responses of said patient;

and said computer-generated visual stimuli are comprised of at least one task selected from the following types of task:
an automated continuous task, a conjunctive search, an orienting flanker task, a shift dual task, or a dichotic listening task.

In a preferred embodiment, the method of treatment additionally comprises a standardization step of computing attentional calculations from said response time and accuracy of response measurements. In such case, preferably, in each task, at least one

of a plurality of attentional calculations is selected for use, according to the nature of said task.

Moreover, in certain embodiments, the method of treatment additionally comprises the step of calculating a personal score for said patient according to a plurality of said response times and accuracy of responses; and outputting a visual message describing said personal score.

Additionally, in certain embodiments, the method of treatment further comprises subjecting said patient to a plurality of auditory stimuli.

Further, according to a preferred embodiment of the method of treatment, the level of difficulty of said visual stimuli and of said at least one task, is adjusted in step (d) by varying at least one parameter selected from: the size of the visual stimuli, the visual similarity of the stimuli to one another, the degree of movement of said stimuli, the spacing between said stimuli, the duration of the display of said stimuli, the ratio of target stimuli to non-target stimuli, the task duration, or the number of locations where the stimuli are displayed. Preferably, each of said parameters can be varied to a plurality of predetermined settings.

There is additionally provided in the present invention, a method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli;
b) measuring the response time and accuracy of response of the patient to said visual stimuli;

c) standardizing said measurements by computing attentional calculations from said response time and accuracy of response measurements;

d) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;

e) adjusting the level of difficulty of said visual stimuli according to the response times and accuracy of responses or according to the attentional calculations of said patient;

and said computer-generated visual stimuli are comprised of at least one task selected from the following types of task: an automated continuous task, a conjunctive search, an orienting flanker task, a shift dual task, or a dichotic listening task.

The present invention additionally discloses a method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli and to auditory stimuli;

b) measuring the response time and accuracy of response of the patient to said auditory stimuli;

c) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;

d) adjusting the level of difficulty of said auditory stimuli according to the response times and accuracy of responses of said patient;

and said auditory stimuli are comprised of a dichotic listening task.

The present invention additionally provides a system for treatment or diagnosis of Attention Deficit Hyperactivity Disorder using the aforementioned methods, comprising;

a) a display monitor for displaying a plurality of visual stimuli;

b) a central processing unit connected to said display monitor;

c) at least one operable switch connected to said central processing unit, which a patient can activate in response to said visual stimuli;

d) programming means for producing a plurality of visual stimuli on said display monitor, for measuring and for committing to memory the response time and accuracy of response of said patient to the visual stimuli; for outputting auditory or visual messages to said patient, wherein said messages reflect the response time and accuracy of response of said patient; and further for adjusting the level of difficulty of said visual stimuli, according to the response times and accuracy of responses of said patient.

According to one embodiment, in the system, the display monitor is selected from a computer monitor, a handheld monitor, a television screen, or a video-game screen.

In certain embodiments of the system, the at least one operable switch is a computer keyboard.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention is herein described, by way of example only, with reference to the accompanying drawings, wherein:

Figure 1 illustrates graphically the attentional calculations computed from accuracy or response time results of a group of 50 children undergoing diagnosis

according to the method of the present invention (as described in Example 2). Results shown are for Stroop tests, for global-local tests, and for a Flankers tests.

Figure 2 illustrates additional results of diagnostic tasks performed in Example 2, namely results of a visual search task, and of a sustained attention test.

Figure 3 illustrates graphically, the "before" and "after" evaluation results, as determined by improvement in math and passage copying, for a group of ADHD subjects who underwent the training regimen (described in Example 3).

Figure 4 illustrates graphically, additional "before" and "after" evaluation results, determined by improvement in executive tasks, and by parents evaluation, for a group of ADHD subjects who underwent the training regimen (described in Example 3).

DETAILED DESCRIPTION OF THE INVENTION

It is appreciated that the detailed description that follows is intended only to illustrate certain preferred embodiments of the present invention. It is in no way intended to limit the scope of the invention, as set out in the claims.

In the method for diagnosis of ADHD, disclosed hereby, a patient is shown a series of computer generated visual stimuli, which constitute a task, to which he/she is asked to respond, for instance, by pressing a key on a computer keyboard. The response time and accuracy of response of the child is measured on each of the tasks. In a preferred embodiment, attentional calculations are computed and calculated, in which the response times and accuracy of responses are standardized using calculations suited to the nature of each task. The object of this step is to remove factors not wholly related to attentional function, and to make the results more statistically accurate.

Performance on each task is then compared to the healthy norm, and based on deviations from norms, an attentional profile is generated. The presence or absence of ADHD or ADD in the patient can thus be diagnosed. Moreover, a comprehensive description of the specific attentional deficits of the patient is provided- a unique feature not found in any prior art.

The computer- generated visual stimuli are comprised of at least nine tasks selected from the following types of task:

1. A Sustained attention test performed using a computer or a video game, is used to test one's level of function of Sustained Attention. The patient is presented with a

long series of stimuli, which are presented briefly, and he is required to respond as fast as possible to a pre-specified target, while withholding responses to all other non-target stimuli. For instance, the patient is to respond to a red horse, while ignoring red dogs and green horses. In ADHD patients, the level of sustained attention, when measured over a period of time, declines rapidly. This is manifested as substantial variance in reaction times, which results from occasional lapses of attention. Furthermore, these patients cannot repress their urge to respond impulsively to nontarget stimuli.

2. A "visual search" and a "flanker task" are used to measure the function of the Selective Attention. Recall that the function of selective attention is the ability to ignore irrelevant distractions. In the visual search, the patient must search for a target stimulus, which is displayed surrounded by a number of "noise" items varying in their similarity to the target. For instance, the subject must respond to a blue square, which is surrounded by red squares and blue circles, which he/she must ignore. In the "flanker" task, subjects are required to respond to one of two possible central targets, flanked by distractors. For example, on a given trial the target is a triangle, and the flankers could be compatible (triangles), incompatible (squares), or nonexistent. Should the selective attention capabilities of the ADHD child be impaired, the response differences between compatible and incompatible trials will deviate from those of healthy individuals. In the present invention, the child's ratings can be compared when "flankers" are compatible and when they are incompatible, regardless of the overall performance, to give an exact measurement of the influence of the flanking distractions. Such a comparison represents a standardization of the results, termed an "attentional calculation". Inclusion of this comparison is an example of how the present invention eliminates the influence of the child's mood on his test ratings: a child who is behaviorally uncooperative on the specific day of the testing will not perform well overall, but his/her difference in response time between trials with compatible flankers and those with incompatible flankers will not be different from normal individuals. Only an ADHD child will show a substantial difference in the response time between the two trial types, as compared to a normal individual. Therefore, the tasks of the present invention are more objective than those of prior art, and more attuned to ADHD children, and to their attentional function capabilities.

3. The Orienting of Attention is a uniquely visual aspect of attention, namely the ability to focus one's attention on a specific area of the visual field, then disengage and focus on another area of the visual field. Certain ADHD children find it difficult to disengage and refocus on a new area in the visual field. This may impair their learning abilities in mathematics and in reading. Two types of tasks are used in the present invention to test the orienting of attention: a cost-benefit paradigm (task) with an endogenous cue, which tests the patient's ability to voluntarily refocus his visual attention. For instance, a cue such as an arrow pointing to the right will be displayed, and shortly after, a target item, to which the subject must respond, will be displayed on the right. In addition, a cost-benefit paradigm (task) with an exogenous cue is used, which tests the involuntary reorienting of one's attention; for instance, a cue such as a brief flashing will show in the right-hand corner of the display monitor, and shortly after a target item will be displayed in that corner. In most people, a flashing will automatically attract their visual attention to that spot.

The most data can be gleaned in the cost-benefit paradigm, from measuring the patient's response after an incorrect cue is displayed; for example, an arrow is shown pointing to the right, however the item, or image, is displayed shortly afterwards on the left side. A healthy individual will have a certain delay before noticing the image and responding to it. The inventors have noted that an ADHD child may take an unusually lengthy amount of time to recover from the "erroneous" cue; being unable to disengage his/her visual attention from the area where he/she expected the image to be displayed. Alternatively, certain ADHD children do not respond to the "valid" cue. Their reaction time to an invalid cue is equal to or is shorter than their reaction time to a valid cue. From this the inventors deduce that in such children the entire pre-cueing event is meaningless. These children have difficulties in orienting. In other ADHD children, the orienting of attention is not impaired, and their ratings of accuracy and response time may be similar to those of healthy individuals.

The child's ratings on the cost-benefit paradigm can be standardized using the following attentional calculation, to give a highly accurate measurement of the functioning of his/her orienting of attention. The time taken to respond to a correctly pre-cued image can be subtracted from the time taken to respond to an

erroneously cued image. Thus the method of the present invention is highly scientific and accurate; the ratings are related to purely attentional defects.

4. The Control of Attention, which represents the ability to integrate and oversee all of the aforementioned attentional functions, is measured using three types of tasks: a Stroop task, a Stroop-like task, and a global-local task:
   a) Stroop tasks have been described above, namely, the patient must name the color ink a word is printed in, regardless of the content of the word and vice versa.
   b) In a Stroop-like task, an arrow is displayed pointing up or down, and located either above or below the center of the display monitor. The patient must either respond "up" or "down" according to the location of the arrow on the display, and ignore the direction that the arrow points towards. At other times the patient is asked to respond "up" or "down" based on the direction the arrow is pointing to, and ignore the location of the arrow relative to the center of the display monitor.
   c) In the global-local task, a large ("global") visual stimulus, such as a square, is displayed. The large stimulus is composed of smaller non-identical elements ('local elements"), such as circles. The patient is instructed to respond to either the identity of the global configuration or the identity of the local elements. In a "switched" global-local task, the patient is instructed to alternate his response from trial to trial between global configurations and local elements.

In addition to the method of diagnosis, the present invention discloses a method of treatment of ADHD. In this method, the ADHD patient must perform at least one task designed to improve one or more of the four attentional functions. The selection of which training tasks the child executes, is ideally derived from his/her performance distribution in the diagnostic tests. The training tasks were constructed based on the following rationale:

a) Potential Transferability - The attentional training tasks are geared towards improving academic and social skills in school and in other daily activities.
b) Interest - The tasks, and their visual displays are sufficiently interesting so as to capture the attention and maintain the concentration and interest of the children for extended periods of time. This is important since the child should preferably

attend approximately 20 training sessions lasting one hour each, during which these tasks are performed.

c) Challenge - The tasks progress in a challenging fashion, which includes a feedback system, with accumulation of points, in order to maximally activate the attentional system and maintain its processing capacity at optimal levels.

d) Improvement - In order to encourage improvement over time, two principles were adopted. First, for each task a variety of levels of difficulty were defined so that the child can move to the next level contingent upon performance. Second, the child receives a tight schedules of feedbacks. Auditory feedback is given on erroneous responses and visual messages are delivered for rapid (positive feedback) and slow (negative feedback) responses based on deviations from the response time and accuracy standards established during a practice period for each individual child.

In the treatment method, at least one (but preferably more than one), training task is assigned to the child out of the following types of training tasks:

1. The Automated Continuous Task (ACT) is designed to improve the function of the sustained attention. This task trains the cognitive system to activate and maintain attention at an optimal level for prolonged periods of time, and to simultaneously inhibit the response system. In general, the subject is presented with a long series of stimuli, and must respond to a pre-specified target (such as a red car) while withholding responses to other stimuli (such as red airplanes, or green cars). This task is performed, while in the background of the display monitor, moving objects distract and create interference. Target-like stimuli appear in abrupt onsets and offsets, at various locations on the display, and at unpredictable time intervals. The level of difficulty is affected by the degree of similarity between the target and the non-target items (such as pink horses vs. green horses), and the extent of the background interference.

To establish levels of difficulty the following variables were manipulated:

i. Presence of peripheral distracting stimuli.

ii. Target-peripheral distractor distance.

iii. Uncertainty of target location

iv. The presence of moving peripheral distractors.

v. Number of targets.

vi. Overall duration of task.

2) The Conjunctive Search Task is designed to improve the function of Selective Attention. In this task the subject is required to search for a target defined by the conjunction of two dimensions), displayed with a background of either stationary or moving distractors. For example, the subject must search for a green smiley boy, displayed among a mixture of red smiley boys and green smiley girls. This task requires the integration of features from two dimensions. As such it activates two dimensional maps in the brain and integrates their relevant features in the master map of locations.

To establish levels of difficulty the following variables were manipulated:

vii. Display size (number of background items among which the subject has to search for the target).

viii. Discrimination difficulty between two features along one dimension (e.g., easy discrimination-red and green smilies; difficult discrimination red and pink smilies)

ix. Extent of movement or jittering of the items.

3) The Orienting Flanker task is designed to improve the function of the Orienting of Attention. In general, the stimulus consists of a string of either letters, digits or shapes. The subject has to identify and respond appropriately to one of two possible target letters or digits within the string, and the target is marked by arrows. For example, the target is defined as being the numbers "1" and "7"; one of these numbers is displayed at the lower corner of the display, flanked by arrows, while at four various other points on the display, four other numbers are displayed. The subject is meant to identify the target number flanked by arrows, by pressing an appropriate button on the computer keyboard. The subject must identify the target number regardless of its position on the display monitor. This task is designed to improve the orienting function by training the attention system to orient itself to a designated target and subsequently disengage and reorient to a new target.

Levels of difficulty are established by manipulating the following variables:

i. Spacing between the items

ii. Duration of presentation

iii. Number of possible locations where the string could appear.

4) The Shift Dual task is designed to improve the function of the Control of Attention. The subject is presented with a global (large) configuration composed of local (small) elements. For example, a large smiley face composed of small cubes, or a large cube outline made out of little smiley faces. The subject is instructed to continuously look for and respond to the smiley faces by pressing a button on the computer keyboard. At different times, the subject is instructed to note and respond to only the global configuration, only the local elements, or both. In a preferred embodiment, the subject is instructed to perform a "block" comprising several repetitions of this task. The blocks can be less difficult, or more difficult, according to the following respective options:

i. A Single block – The subject is to search, for instance, for only global configurations, while ignoring the local elements. (Alternatively, he must search for local elements only, and ignore the global configurations). This block is the least difficult to perform.

ii. A Dual block – The subject is to respond to the presence of the target element, regardless its display size. He must divide his attention between the global configurations and the local elements, and search, for instance, for a large or a small smiley face.

iii. An Ordered Shift block – The subject must shift before each repetition of the task, from a global, to a local, to a dual search, in a predetermined order which is maintained throughout the block.

iv. A Random Shift block - The subject must shift between the three types of searches (global, local, or dual searches), in a random unpredictable fashion according to instructions displayed before each repetition.

This task is designed to strengthen the attentional control by training subjects to swiftly switch between focusing, and dividing their attention.

5) The Dichotic Listening task- The subject is presented with two simultaneous streams of auditory messages transmitted to both ears (i.e., each ear receives both messages). In addition he observes the display monitor. The subject may be instructed to focus on one auditory message, and ignore the remaining information. Alternatively, he may be instructed to divide his attention between the two auditory messages (for instance, to respond to an auditory target heard in either message). In a third option, he is instructed to divide his attention between the auditory messages and the visual message presented on the display monitor. In all cases, the subject must respond as fast as possible to the appearance of a target item. The subject may be instructed that target is broad, for instance, any item considered to be furniture, or any item belonging to the category of fruits.

The training method was designed to assure the subject's improvement in training, with gradual progression of the subject up through the various levels of difficulty. He is motivated by a tight schedule of feedbacks. Special attention was given during design of the levels of difficulty, to:

a. The selection of the parameters which determine the difficulty level b. The degree of manipulation of each such parameter. In a preferred embodiment, there are various settings for each such parameter. c. The ordering of combinations of difficulty levels across variables (i.e., deciding which parameter is introduced first) d. the selection of performance criteria for advancing to the next level of difficulty.

For each task the specific parameters of difficulty were selected, that, when manipulated, were most likely to produce a substantial effect on the subject's performance.

For each such parameter the inventors selected specific levels of difficulty. The difference between any two adjacent levels was sufficiently large to require a reasonable amount of effort. This is to encourage the subject to optimal performance, and reward him by his consequently advancing to the next difficulty level. The difference between any two adjacent levels was not too large, for this

would require too much time for improvement, would discourage subjects and consequently minimize their chance for improvement.

In each training task, the parameters were assessed and manipulated according to their difficulty. For example, in the Visual Search Task increasing the number of distractors has a much more detrimental effect on performance than increasing the speed of movement of items. Thus, display size is a more "difficult" variable than movement. The general idea was to change levels of difficulty first for the easiest variable, then for the next easiest variable and so on.

The decisions taken in establishing the above parameters were based on *a priori* knowledge gained during extensive experiments during which healthy subjects performed visual attention experiments, as well as empirical data obtained with ADHD subjects during the assessment phase.

According to one preferred embodiment, a personal score is given to each child during each training session. The child performs a block of tasks, which includes a series of repetitions of a specific type of task, and at the end of this block, he is rated according to his performance, with the rating, or personal score, for this block, being displayed on his monitor. This display is highly important for increasing his motivation; and serves to challenge him when he next performs these tasks. Four possible outcomes exist each time a task is performed, and the child is rated accordingly:

a) erroneous answer

b) correct answer, response time is equal to average

c) correct answer, response time is above average (faster than average)

d) correct answer, response time below average (slower than average).

According to a preferred embodiment, attentional calculations are included in the treatment method. For each task the subject begins with a practice block during which a standard distribution is established and its statistical properties of central tendency and dispersion serve as the basis for subsequent advancement in levels of difficulty. (Subjects advance in difficulty levels according to pre-specified criteria based on accuracy and reaction time, after they are adjusted to each individual subject.) Advancement up through the various levels of difficulty can be dependant upon the child's results after attentional calculations have been computed and factored into the equation. The response time results and

accuracy of response results are thus standardized, and the non-attentional factors which contribute to them are removed, before the level of difficulty is adjusted. The performance criteria are different for each difficulty level and depend on the nature of the specific task, and the specific parameters manipulated. For example, in the orienting flanker task, reducing the duration of the presentation produces a substantial effect on accuracy but a minimal effect on the reaction time (RT), whereas reducing the spacing between the items primarily affects the reaction times. Therefore, advancing through the levels of difficulty when the duration of the presentation is reduced, is based on maintaining an optimal level of accuracy. Similarly, advancing up through the levels of difficulty, when the spacing between the items is reduced, is based on RT performance.

The method of treatment hereby disclosed, is highly attuned to ADHD children. Prior art methods of treatment do not include such a highly elaborate scheme of rewards and feedback. The possibility to advance through the various levels of difficulty provides the child with the exact degree of challenge necessary for that particular child (as is seen and provided for based on his performance on the practice session). The child is given tasks which are relevant to the areas of attention which he/she needs to improve, at a level of difficulty that is appropriate for him/her to succeed at, despite the fact that at school he/she is often unsuccessful, and may suffer from low self esteem. Immediate auditory or visual feedback messages are displayed for the child, so that though he/she is in fact learning and training his attentional system, he/she enjoys an attractive experience similar to that of a video game. The training method has been proven to improve basic academic skills such as math performance, passage copying, reading comprehension, and instructional-organizational tasks, as is shown in the following examples section.

EXAMPLES

EXAMPLE 1

Five subjects underwent the diagnostic and training phases. Included below are their previous diagnosis results, for comparison to the diagnosis reached using the diagnosis method of the present invention. The diagnosis using this method describes the child's level of impairment in each of the four elements of attention. A training

regimen of approximately 20 one-hour training sessions was designed for each child, with emphasis placed on the attentional areas in which he/she was the most deficient. The training tasks were selected accordingly, and the level of difficulty was adjusted individually to each subject. The child's academic improvement after completion of the training sessions was evaluated during a 90 minute session, during which his/her scoring was rated for passage copying, reading comprehension, math exercises and verbal math problems. The child was also rated on a series of complex instructional-organizational tasks.

Subject 1 (1071)

Former diagnosis: Diagnosed as ADHD/IA according to DSM VI criteria. Grade in TOVA: -4.84.

Overall diagnosis according to the present invention: Major problems in sustained attention and control of attention, minor problem in selective attention. In particular:

Sustained Attention - computerized test indicate a severe difficulty in preserving attention for a prolonged period. Suffers from substantial fluctuations in performance, as well as highly frequent omissions and commissions (commissions are erroneous, or impulsive responses to non-target stimuli).

Selective Attention - A minor problem in selective attention and target localization, revealed by anomalous faster responses to targets flanked by incompatible distractors, than to targets flanked by compatible distractors.

Control of Attention – A highly consistent deficit in control, expressed as the difficulty in suppressing irrelevant responses during all attentional control tasks.

Training: Participated in 19 sessions.
31% improvement in passage copying, and 33% improvement in instructional-organizational tasks.

Subject 2 (1001)

Former diagnosis: Difficulty in attending to some academic tasks, lack of organization. Medication prescribed: Ritalin.

Overall diagnosis according to the present invention: Major problems in sustained attention, control of attention and orienting of attention. In particular:

Sustained Attention – Substantial fluctuations and false alarms indicating distractibility and impulsivity.

Orienting of Attention - enormous differences in responding to cued and non-cued targets with both endogenous and exogenous cueing. Results indicate problems of disengagement in both voluntary and involuntary attention.

Control of Attention - Problems in control of attention expressed primarily as difficulties in ignoring incongruent stimuli in both the Stroop and Stroop-like tasks.

Training: Participated in 10 sessions.
52% improvement in passage copying. 31% improvement in math performance, 33% improvement in reading comprehension.

Subject 3 (1041)

Former diagnosis: restlessness, deficits in attention and concentration.

Overall diagnosis according to the present invention: Major problems in selective attention and orienting of attention; minor problems in control of attention. In particular:

Selective Attention - a substantial difficulty in ignoring incongruent flankers, for both near and even for relatively far distractors.

Orienting of Attention - Normal performance with endogenous cueing. No response to the cost-benefit paradigm with exogenous cueing, which indicates a severe problem in the automatic mechanism of orienting attention.

Control of Attention – Normal performance in the various control tasks but some problems in switching between attention modes.

Training: Participated in 18 sessions. 27% improvement in math performance. 30% improvement in passage copying. 50% improvement in reading comprehension. 33% improvement in instructional-organizational tasks.

Subject 4 (1161)

Former diagnosis: restlessness, apprehension, and lack of organization.

Overall diagnosis according to the present invention: Major problems in control of attention and sustained attention, intermediate problems in orienting of attention and selective attention. In particular:

Sustained Attention - severe problems in distractibility and impulsivity. Computerized task shows enormous fluctuations as well as high rates of false alarms. Manual version shows fluctuations and very slow performance.

Selective Attention- Poor performance with incompatible near and far flankers.

Orienting of Attention - orienting problems with exogenous cueing and disengagement problems in endogenous cueing.

Control of Attention - Abnormally faster responses for incongruent than for congruent stimuli in both the Stroop and Strooplike tasks. Inability to ignore local elements on the Global-local task.

Training: Participated in 18 sessions.
22% improvement in math performance. 28% improvement in passage copying. 50% improvement in reading comprehension.

Subject 5 (1221)

Former diagnosis: significant difficulties in attentional processes. Difficulty in balancing attention even under medication.

Overall diagnosis according to the present invention: Major problems in sustained attention and orienting of attention, intermediate problem in control of attention. In particular:

Sustained Attention - Performance in both computerized and manual tasks shows substantial fluctuations, omissions and commissions indicating severe distractibility and impulsivity.

Orienting of Attention- Both endogenous and exogenous measurements suggest problems in involuntary and voluntary disengaging of attention.

Control of Attention – The Stroop-like task revealed a certain difficulty in suppressing irrelevant responses.

Training: Did not yet complete the training phase.

EXAMPLE 2

Two groups of subjects were tested using the diagnostic tasks; an experimental group of 50 children diagnosed as ADD or ADHD and a control group of 30 normal age-matched children. All subjects performed all of the diagnostic tasks during five to six sessions lasting 90 minutes each. In each of the tests we measured the accuracy and response time (RT) for each subject. Importantly, performance was not evaluated according to overall RT or accuracy but based on differences between various conditions within each test according to its unique characteristics. These performance distributions enabled isolation and specification of pure attentional deficits. For example, a given distribution measuring selective attention was derived from differences between the time taken to respond to a target flanked by incompatible distractors minus the time taken to respond to the target without distractors; a given distribution measuring orienting of attention was based on the time taken to respond to a target at an unexpected location minus the time taken to respond to a target appearing at an expected location. Prior to testing, the various parameters were continuously modified so as to increase the sensitivity (i.e., discriminating power) of each test, and the single most sensitive task for each attentional function was selected.

Results

Referring to Figure 1 and Figure 2, each graph portrays accuracy (ACC) or response time (RT) measurements taken for all ADHD children participating in the diagnosis experiment. Each graph describes a different measurement of a task, with each subject being represented by an open circle. The Y-axis relates to the value measured (accuracy or response time) for a given measurement in a given task, after statistical analysis was carried out to standardize each measurement so that it relates solely to attentional performance. The X-axis is designed to arbitrarily distribute the results along this axis, to aid visually in viewing the results.

In each figure the two horizontal dashed lines delineate the central area of normal performance. This area was determined individually for each measurement of each

task based on statistical analysis of results obtained from healthy (normal) subjects. ADHD subjects falling within the area bounded by the dashed lines exhibited normal performance on a given measurement of a given task. Subjects falling outside this area (above or below it) deviate from normal performance on the given measurement.

For each measurement on each of the tasks, the control group exhibited fairly dense performance distributions (i.e., small differences among subjects), whereas the clinical group produced significantly more dispersed distributions with substantial deviations in both directions. We then developed statistical methods to isolate those clinical subjects that deviate sufficiently from the norm; these were identified as being deficient on a given test. In general, each subject deviating from the mean of the control distribution by more then 1.64 standard deviations in either direction was considered deficient on a given measurement.

For each subject we then constructed an attentional profile based on his/her performance in each of the tasks. We have obtained a variety of profiles for the ADHD subjects. Preliminary experiments have shown that in general, deficits in sustained attention and control of attention are somewhat more frequent than those in orienting attention and selective attention. The chart below summarizes the attentional profiles for the first group of 31 ADHD subjects. The chart indicates the extent of deficit (i.e., deviation from the norm) of each function for each child (white background = no deficit; light gray = mild deficit; gray = intermediate deficit; dark gray = severe deficit).

Attentional Profiles: ADHD experimental Group No 1

ID	Selective Attention	Orienting Attention		Sustained Attention	Control Of Attention
		Orienting	Disengagement		
1001			**	***	***
1011	*			***	***
1021	***	*		**	**
1031	*	*			**
1041	***	***			*
1051	**			***	*
1061	**			***	*
1071	*			***	***
1081				**	***
1091			*		**
1101	***			***	**
1111	*		***	***	***
1121	***	**			**
1131	***		*		*
1141	**				***
1151			*	**	***
1161	**	*		***	
1171			*	*	***
1181	*		**	***	**
1191	***		*	*	**
1211	**	*			*
1221			**	***	*
1231			*	***	*
1261	*			*	**
1271				**	*
1281				***	*
1311	**		*		**
1351	*			***	***
1211	**	*			*
1381	**		*		*
1391	*	*			**

The diagnostic research has proven very successful. We were able to clearly distinguish between ADHD and normal subjects, and more importantly, to identify

deficient as well as normal attentional functions in ADHD subjects, hence, providing a unique attentional profile for each individual child.

EXAMPLE 3

A group of 15 ADHD children was subjected to the training tasks, and their performance and improvement over time were compared to a control group of 5 children. The first phase of the training program was carried out over a period of eight-ten weeks consisting of two one-hour sessions per week. During each session subjects performed a selection of tasks from the ones described above. Within each task subjects advanced in the levels of difficulty specified above, according to their gradual progress as expressed in speed and accuracy performance.

In order to evaluate the success of our program, subjects were tested on several criteria consisting of academic and general attentional tests before and after training. Improvement on these tasks (relative to natural progress of control subjects) served as an indication for the success of our program. This final evaluation required a full 90-min session. The control group consisted of ADHD children who participated in sessions of the same frequency, length and format except that instead of performing the training tasks they played various computer games during the session. This comparison allows for as pure as an assessment as possible as to the unique contribution of our training so that improvement in criteria could be attributed solely to the success of our program rather than to other extraneous variables associated with natural progress over time or with the testing environment.

The following training evaluation tests were used as criteria for evaluating our training program: Academic tests consisted of passage copying, reading comprehension, math exercises, math verbal problems. General attentional tests consisted of organization and planning of complex activities – subjects were presented with objects varying in identity, color, size and relative location, and were instructed to perform various complex activities with selected objects.

Referring to Figure 3, and Figure 4, the evaluation results are shown for the group of ADHD subjects who underwent the training regimen. Each diagram depicts the average results achieved by the group for a particular evaluation test,

with the left-hand column representing the results obtained before the training regimen was started ("pre-training"), and the right-hand column representing results obtained after all sessions of the training regimen were completed ("post-training"). The statistical significance of the results was determined by T-test, with the level of significance for each evaluation test depicted in a box at right by the value of α. Also shown in the box at right, is the percentage of children out of the group, that showed marked improvement.

Most subjects showed substantial improvement in each of the tests: reading comprehension, passage copying, math and organization and planning. Furthermore, as shown in Figure 4 (pie graph), the progress evaluation as rated by parents of the ADHD children, ranged mostly from substantial improvement (50% of subjects) to mild improvement (30% of subjects). Clearly, the results indicate remarkable improvement after only 8-10 weeks of training.

EXAMPLE 4: Controlling the level of difficulty in the OF (Orienting and Flanker) Task

The following variables and parameters were used to control and manipulate the levels of difficulty for this task:

Exposure Duration
Until response
500 msec.
100 msec.

Spacing
Five spaces (item widths) between adjacent items
Three spaces between adjacent items
One space between adjacent items

Stimulus Location
Stimulus appears either to the right or to the left of fixation
Stimulus appears in one of six possible locations surrounding fixation.

The most difficult variable is spacing, the second most difficult variable is exposure duration, and the easiest variable is stimulus location.

Hence, the levels of difficulty in the OF task proceeded in the following order:

Difficulty	Spacing	Exposure Duration	Stimulus Location
Level 1	5 spaces	Until response	2 possible locations
Level 2	5 spaces	Until response	6 possible locations
Level 3	5 spaces	500 msec.	6 possible locations
Level 4	5 spaces	100 msec.	6 possible locations
Level 5	3 spaces	100 msec	6 possible locations
Level 6	1 space	100 msec	6 possible locations

This sequence of difficulty levels trains the subjects first to attend to various locations in the visual field, then to process information presented for brief time durations, then to focus attention on the target while inhibiting processing of nearby distractors.

CLAIMS

1. A method for comprehensive and sensitive diagnosis of Attention Deficit Hyperactivity Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli; and said computer generated visual stimuli are comprised of at least nine tasks selected from the following types of task: a sustained attention test, a visual search, a flanker task, a cost-benefit paradigm with endogenous cues, a cost-benefit paradigm with exogenous cues, a stroop task, a stroop-like task, a global-local task or a switched global-local task;

b) measuring the response time and accuracy of response of the patient for each of said tasks;

c) comparing said measurements for each task with measurements generated from healthy individuals;

d) generating an attentional profile for the patient based on said comparison;

e) diagnosing the presence or absence of ADHD or ADD in said patient.

2) A method according to claim 1, additionally comprising a standardization step of computing attentional calculations from said response time and accuracy of response measurements, and said attentional calculations are utilized in step (c) in said comparison.

3) A method according to claim 2, wherein in each task, at least one of a plurality of attentional calculations is selected for use, according to the nature of said task.

4. A method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli;

b) measuring the response time and accuracy of response of the patient to said visual stimuli;

c) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;

d) adjusting the level of difficulty of said visual stimuli according to the response times and accuracy of responses of said patient;

and said computer-generated visual stimuli are comprised of at least one task selected from the following types of task:
an automated continuous task, a conjunctive search, an orienting flanker task, a shift dual task, or a dichotic listening task.

5) A method according to claim 4, additionally comprising a standardization step of computing attentional calculations from said response time and accuracy of response measurements.

6) A method according to claim 5, wherein in each task, at least one of a plurality of attentional calculations is selected for use, according to the nature of said task.

7) A method according to claim 4, additionally comprising the step of calculating a personal score for said patient according to a plurality of said response times

and accuracy of responses; and outputting a visual message describing said personal score.

8) A method for treatment according to claim 4, further comprising subjecting said patient to a plurality of auditory stimuli.

9) A method for treatment according to claim 4, wherein the level of difficulty of said visual stimuli and of said at least one task, is adjusted in step (d) by varying at least one parameter selected from: the size of the visual stimuli, the visual similarity of the stimuli to one another, the degree of movement of said stimuli, the spacing between said stimuli, the duration of the display of said stimuli, the ratio of target stimuli to non-target stimuli, the task duration, or the number of locations where the stimuli are displayed.

10) A method for treatment according to claim 9, wherein each of said parameters can be varied to a plurality of predetermined settings.

11) A method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli;

b) measuring the response time and accuracy of response of the patient to said visual stimuli;

c) standardizing said measurements by computing attentional calculations from said response time and accuracy of response measurements;

d) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;

e) adjusting the level of difficulty of said visual stimuli according to the response times and accuracy of responses or according to the attentional calculations of said patient;

and said computer-generated visual stimuli are comprised of at least one task selected from the following types of task: an automated continuous task, a conjunctive search, an orienting flanker task, a shift dual task, or a dichotic listening task.

12) A method for treatment of Attention Deficit Hyperactivity Disorder or Attention Deficit Disorder comprising;

a) subjecting a patient to a plurality of computer generated visual stimuli and to auditory stimuli;

b) measuring the response time and accuracy of response of the patient to said auditory stimuli;

c) outputting auditory or visual messages to said patient reflecting the response time and accuracy of response of said patient;

d) adjusting the level of difficulty of said auditory stimuli according to the response times and accuracy of responses of said patient;

and said auditory stimuli are comprised of a dichotic listening task.

13) A system for treatment or diagnosis of Attention Deficit Hyperactivity Disorder comprising;

a) a display monitor for displaying a plurality of visual stimuli;

b) a central processing unit connected to said display monitor;

c) at least one operable switch connected to said central processing unit, which a patient can activate in response to said visual stimuli;

d) programming means for producing a plurality of visual stimuli on said display monitor, for measuring and for committing to memory the response time and accuracy of response of said patient to the visual stimuli; for outputting auditory or visual messages to said patient, wherein said messages reflect the response time and accuracy of response of said patient; and further for adjusting the level of difficulty of said visual stimuli, according to the response times and accuracy of responses of said patient.

14) A system according to claim 13, wherein said display monitor is selected from a computer monitor, a handheld monitor, a television screen, or a video-game screen.

15) A system according to claim 13, wherein said at least one operable switch is a computer keyboard.

16) A system according to claim 13, wherein said visual stimuli produced by said programming means are selected from the following types of task: a sustained attention test, a visual search, a flanker task, a cost-benefit paradigm with endogenous cues, a cost-benefit paradigm with exogenous cues, a stroop task, a stroop-like task, a global-local task, a switched global-local task, an automated

continuous task, a conjunctive search, an orienting flanker task, a shift dual task, or a dichotic listening task.

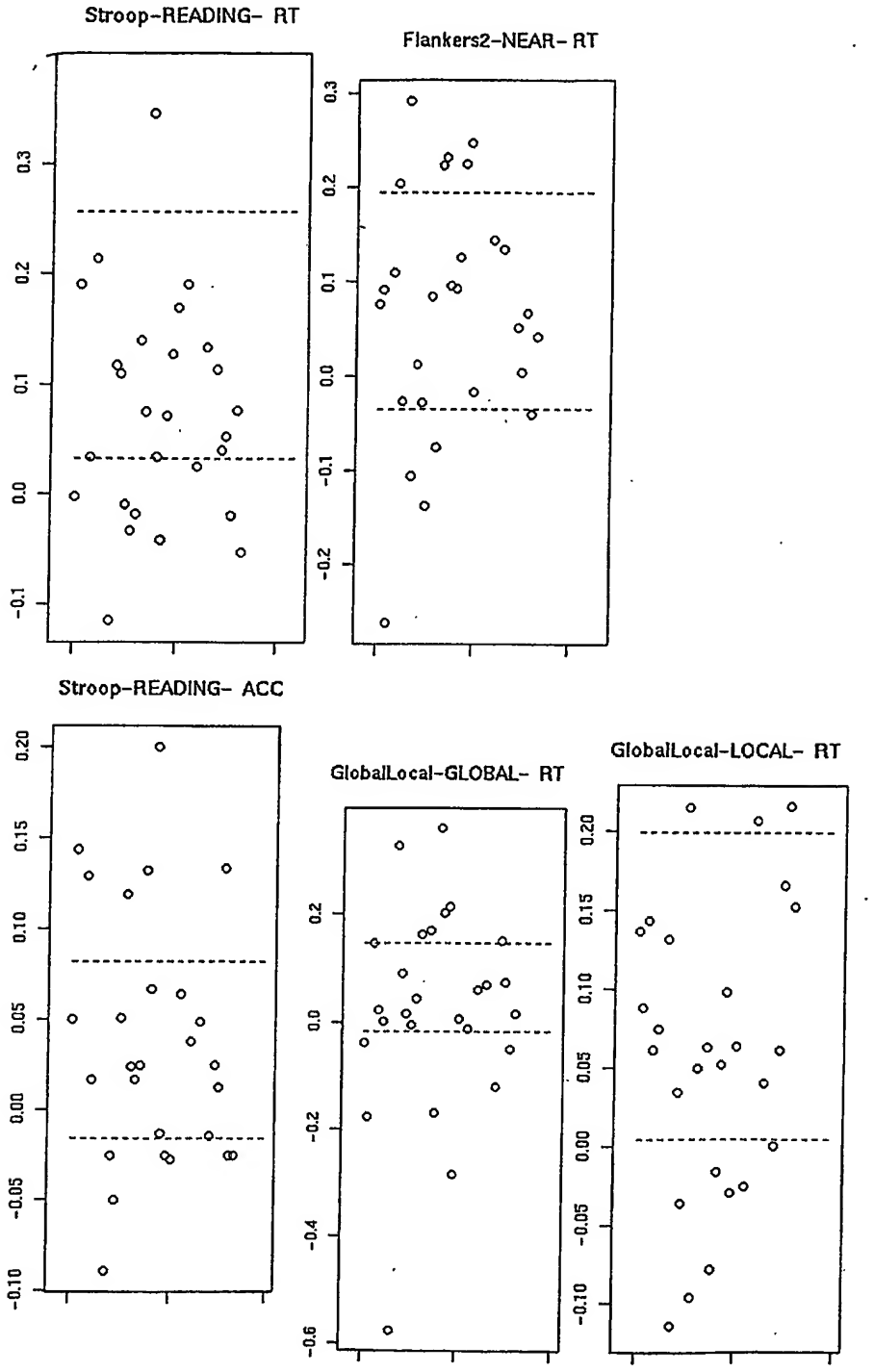

Stroop-READING- RT
Flankers2-NEAR- RT
Stroop-READING- ACC
GlobalLocal-GLOBAL- RT
GlobalLocal-LOCAL- RT

FIGURE 1

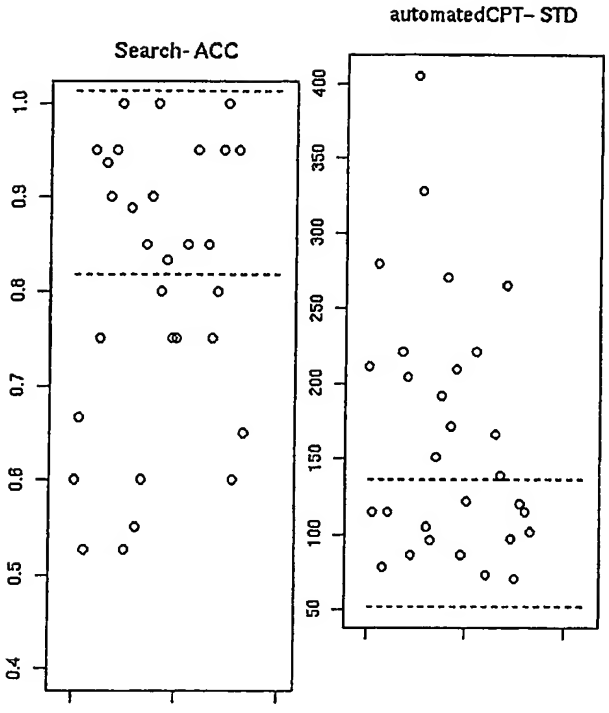
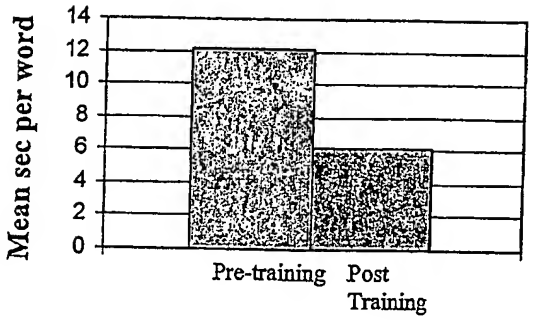

Search- ACC
automatedCPT- STD
1.0
0.9
0.8
0.7
0.6
0.5
0.4
400
350
300
250
200
150
100
50

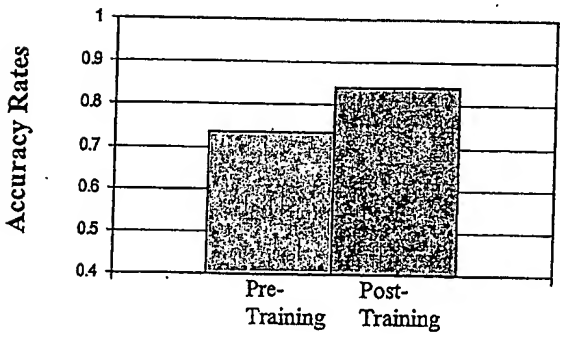
FIGURE 2

Passage Copying

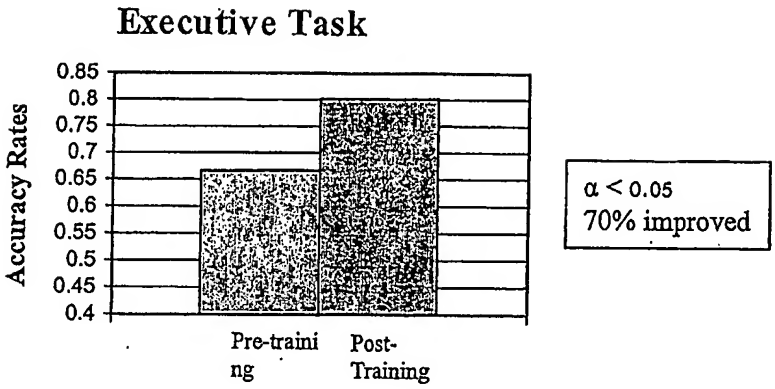


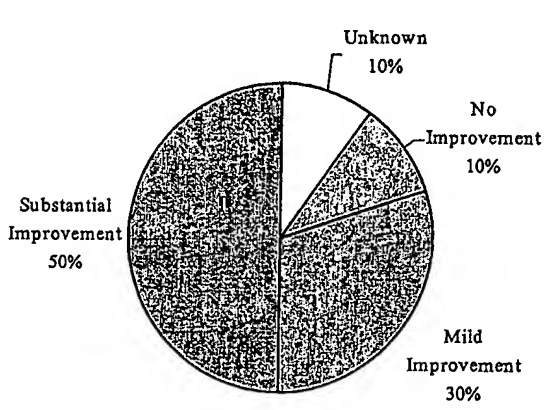
$\alpha < 0.05$
89% improved

Math



$\alpha < 0.05$
67% improved


Executive Task
Accuracy Rates
0.85
0.8
0.75
0.7
0.65
0.6
0.55
0.5
0.45
0.4
Pre-traini ng
Post-Training
α < 0.05
70% improved


Parents' Evaluations
Unknown 10%
No Improvement 10%
Substantial Improvement 50%
Mild Improvement 30%

INTERNATIONAL SEARCH REPORT

Internationa lication No
PCT/IL 03/00173

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/16 G09B19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B G09B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 165 126 A (MERZENICH MICHAEL M ET AL) 26 December 2000 (2000-12-26) column 6, line 60 -column 7, line 50 column 13, line 27 - line 67; figures ---	13-16
A	US 6 053 739 A (SULLIVAN THOMAS D ET AL) 25 April 2000 (2000-04-25) cited in the application column 3, line 8 - line 27 column 13, line 15 -column 14, line 57 ---	13-16
A	US 6 334 778 B1 (BROWN STEPHEN J) 1 January 2002 (2002-01-01) column 11, line 62 -column 12, line 16 column 15, line 20 -column 16, line 18 column 17, line 17 -column 18, line 63 --- -/--	13-16

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 June 2003	04/07/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Manschot, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL 03/00173

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 978 303 A (LAMPBELL AL) 18 December 1990 (1990-12-18) column 3, line 3 -column 5, line 67	13-15

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Internati application No.
PCT/IL 03/00173

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-12
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body and method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internationa cation No
PCT/IL 03/00173

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